REMARKS

Claims 51, 55-59, 63-71 and 77-121 were pending in the instant application. By this amendment, claims 51, 56, 69-71, 79-82, 93-98, and 107-109 have been amended to clarify the invention. In particular, claims 51, 56, 79-82 were amended to more distinctly claim the invention, and claims 69-71, 93-98, and 107-109 were amended to recite methods which are "potentially" useful for treatment of a particular disease. Support for the amendment can be found in Section 5.11 of the application, particularly page 88, lines 12-15, which discloses that compounds and methods that increase or enhance the activity of the HSP receptor can be used to treat immune disorders such as immunodeficiency syndromes, cancers or infectious diseases. As such, no new matter has been added.

1. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, FOR INDEFINITENESS, SHOULD BE WITHDRAWN

Claims 69-71, 93-98, and 107-109 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner contends that the claims are indefinite because there is no indication in the claims that the molecule identified would necessarily result in the treatment of the various recited diseases in humans. In response, the claims have been amended by adding the word "potentially" to the preamble, according to the Examiner's suggestion. As such, Applicant submits that the rejection has been overcome and respectfully request its withdrawal.

2. THE REJECTION UNDER 35 U.S.C. § 102(b) FOR ANTICIPATION SHOULD BE WITHDRAWN

Claims 51, 67, 77, 78, 103, 110, and 111 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Erickson *et al.* (U.S. Patent No. 5,525,490, "Erickson"). The Examiner's rejection is based on the disclosure in Erickson of methods for screening for

small molecule inhibitors that disrupt the interaction between Hsp90 and the hormone domain of the estrogen receptor. The Examiner alleges that the estrogen receptor falls within the meaning of heat shock protein receptor (HSPR) as set forth in the instant specification. Based on this contention, the Examiner asserts that Erickson discloses purified HSPR positive cells, screening methods for inhibitors for the intermolecular binding of two interacting polypeptides using compound libraries and peptide expression libraries, and the therapeutic use of identified small molecule inhibitors, peptides, and compounds. Thus, according to the Examiner, Erickson discloses all of the elements of the claimed screening methods. Applicant asserts that this rejection is in error, for the reasons set forth below.

According to the applicable case law, in order for a reference to anticipate a claim, each and every element of the claim must be disclosed in that one reference. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565 (Fed. Cir. 1985). "Anticipation under Section 102 can be found only if a reference shows exactly what is claimed . . ." *Structural Rubber Prod. Co. v. Park Rubber Co.,* 749 F.2d 707 (Fed. Cir. 1984).

Applicant asserts that the rejection is in error because neither the estrogen receptor nor its hormone binding domain of Erickson is an HSPR, as defined in the specification. HSPRs are described in the specification as *cell surface* receptors for heat shock proteins which recognize and bind to HSPs and *are associated with the cell membranes of a subset of macrophages and dendritic cells* (specification at page 1, lines 12-20; emphasis added). HSPRs are further explicitly defined as protein receptors which (a) specifically bind HSPs, and which can bind HSPs in non-covalent complexes with antigenic peptides; and (b) *are associated with the cell membranes of macrophages and dendritic cells that are involved in antigen presentation* (specification at page 10, line 31, to page 11, line 5; emphasis added).

The estrogen receptor is <u>not</u> an HSPR, as defined in the specification, because

it is not a cell surface receptor or even associated with cell membranes. The estrogen receptor is a member of the steroid/thyroid hormone receptor superfamily of nuclear receptors (for review, *see* Alberts *et al.*, Molecular Biology of the Cell, 3rd Ed., 1994, Garland Publishing, Inc. NY, pp. 729-731 ("Alberts"); reference "CI" in the Information Disclosure Statement ("IDS") submitted herewith; and Tsai & O'Malley, Annu. Rev. Biochem., 1994, 63:451-486 ("Tsai & O'Malley"); reference "CL" in the IDS submitted herewith). Steroid nuclear receptors are intracellular transcription factors located either in the cytoplasm or nucleus in inactive apoprotein form (Tsai & O'Malley, page 452, lines 3-5) and have lipophilic ligands that diffuse directly across the plasma membrane of target cells and interact with and activate the intracellular receptors (see Alberts at page 729, lines 13-15).

Moreover, the Hsp90-estrogen receptor interaction is not even a ligand-receptor interaction. As noted in the specification, heat shock proteins perform a variety of cellular functions, including chaperone functions such as folding, assembly, transfer and trafficking of proteins in normal cells, and protecting cells against heat shock and other physiological stresses (specification at page 2, lines 17-31). In the case of the estrogen receptor-Hsp90 interaction, Hsp90 functions as a molecular chaperone, interacting with the unliganded estrogen receptor (aporeceptor), altering its conformation in such a way so as to facilitate the ability of the estrogen receptor to bind its ligand (*e.g.*, estradiol), leading to increased interaction with co-activators, DNA binding and target gene transcriptional activation (see Picard *et al.*, Nature 348: 166-168, p. 167, col 2, last ¶; reference "CJ" in the IDS submitted herewith; reviewed by Pratt and Toft, 1997, Endocr Rev. 1997, 18:306-60; reference "CK" in the IDS submitted herewith). Thus, the estrogen receptor is found in the cytoplasm complexed with Hsp90 in the absence of hormone, where, upon hormone binding, Hsp90 dissociates and the receptor is transferred to the nucleus where it acts as a transcriptional regulator (Tsai and O'Malley, paragraph bridging page 466 and 467.

Therefore, the estrogen receptor is clearly not an HSPR, as defined in the instant specification. Neither the estrogen receptor nor the ligand binding domain thereof is associated with a cell membrane or involved in antigen presentation, as required by the definition of an HSPR in the specification of the instant application. Rather, Hsp90 acts in the cytoplasm as a chaperone for the estrogen receptor. Thus, the estrogen receptor is a cytoplasmic and nuclear receptor, not a cell surface receptor -- and as such, is not an HSPR.

Thus, Erickson lacks a required claim element of each of claims 51, 67, 77, 78, 103, 110, and 111, *i.e.*, an HSPR, and, as such, does not anticipate the claimed invention. Accordingly, in view of the above remarks, Applicant respectfully submits that the rejection under 35 U.S.C.§ 102(b) should be withdrawn.

CONCLUSION

Applicant respectfully requests that the present remarks and amendments be entered and made of record in the instant application.

Applicant notes that the Examiner has indicated that Claims 56, 58, 59, 63-66, 79-92, 99-102 and 112-115 are allowed. Applicant estimates that the remarks and amendments made herein now place the pending claims in condition for allowance.

It is believed that no fee is required for filing this response. In the event a fee is required, please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

Date: September 30, 2003

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Enclosures